

## WHAT IS CLAIMED IS:

1. A hybrid polypeptide immunogen comprising a modified ORF0657n sequence segment at least about 100 amino acids in length, wherein said modified sequence 5 segment comprises one or more alterations that increases sequence similarity to SEQ ID NO: 1.

2. The hybrid polypeptide of claim 1, wherein said modified sequence segment comprises at least about 100 amino acids of a modified amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and 10 SEQ ID NO: 6, provided that said modified amino acid sequence contains at least 8 amino acid alterations that increase sequence similarity to SEQ ID NO: 1.

15 3. The hybrid polypeptide of claim 3, wherein said modified amino acid sequence is SEQ ID NO: 2 containing 8 to 100 amino acid alterations that increase sequence similarity to SEQ ID NO: 1.

4. The hybrid polypeptide of claim 2, wherein said modified amino acid sequence has the following sequence:

X<sub>1</sub>-AIKNPAI-X<sub>2</sub>- DK-X<sub>3</sub>-H-X<sub>4</sub>-APN-X<sub>5</sub>- RPIDFEMK-X<sub>6</sub>-X<sub>7</sub>-X<sub>8</sub>-G-X<sub>9</sub>-  
20 QQFYHYAS-X<sub>10</sub>-V-X<sub>11</sub>- PARVIFT-X<sub>12</sub>-X<sub>13</sub>-K-X<sub>14</sub>-IELGLQ-X<sub>15</sub>-X<sub>16</sub>-X<sub>17</sub>-  
X<sub>18</sub>-W-X<sub>19</sub>-KFEVYEGDKKLP-X<sub>20</sub>- KLVSYD-X<sub>21</sub>-X<sub>22</sub>-KDYAYIRFSVSNGT-  
X<sub>23</sub>-X<sub>24</sub>-VKIVSSTH-X<sub>25</sub>-X<sub>26</sub>-X<sub>27</sub>-N-X<sub>28</sub>-X<sub>29</sub>-EKYDYTLML-X<sub>30</sub>- FAQPIYN-X<sub>31</sub>-X<sub>32</sub>-  
DK-X<sub>33</sub>-X<sub>34</sub>-X<sub>35</sub>- EEDY-X<sub>36</sub>-X<sub>37</sub>-X<sub>38</sub>- KLLAPYKKAKTLERQVY EL-X<sub>39</sub>- K-X<sub>40</sub>- Q-  
X<sub>41</sub>-KLPEKLKAELYKKKL-X<sub>42</sub>-X<sub>43</sub>-T-X<sub>44</sub>- KAL-X<sub>45</sub>-X<sub>46</sub>-QVKSA-X<sub>47</sub>- TEFQNV-X<sub>48</sub>-  
25 PTN-X<sub>49</sub>-K-X<sub>50</sub>- TDLQ-X<sub>51</sub>-X<sub>52</sub>-X<sub>53</sub>-X<sub>54</sub>-VV-X<sub>55</sub>-ESVEN-X<sub>56</sub>-ES-X<sub>57</sub>-MDTFV-X<sub>58</sub>-  
HPIKT-X<sub>59</sub>-X<sub>60</sub>-LNGKKY-X<sub>61</sub>-VM-X<sub>62</sub>- TTND-X<sub>63</sub>-YWKDF-X<sub>64</sub>- VEG-X<sub>65</sub>- RVRT-  
X<sub>66</sub>- SKD-X<sub>67</sub>- KNN-X<sub>68</sub>- RT-X<sub>69</sub>- IFPY-X<sub>70</sub>- EGK-X<sub>71</sub>-X<sub>72</sub>-YDAIVKV-X<sub>73</sub>- VKTI-X<sub>74</sub>-  
Y-X<sub>75</sub>-GQYHVRI-X<sub>76</sub>- DK-X<sub>77</sub>-X<sub>78</sub>-X<sub>79</sub>

30 wherein

X<sub>1</sub> is either E or a D alteration;

X<sub>2</sub> is either K or an I alteration;

X<sub>3</sub> is either D or an E alteration;

X<sub>4</sub> is either S or a T alteration;

35 X<sub>5</sub> is either S or a W alteration;

- X<sub>6</sub>-X<sub>7</sub>-X<sub>8</sub> is either KKD or NDK alterations;  
X<sub>9</sub> is either T or an E alteration;  
X<sub>10</sub> is either S or a T alteration;  
X<sub>11</sub> is either K or an E alteration;
- 5 X<sub>12</sub> is either D or a K alteration;  
X<sub>13</sub> is either S or a T alteration;  
X<sub>14</sub> is either E or an I alteration;  
X<sub>15</sub> is either S or a T alteration;  
X<sub>16</sub> is either G or an A alteration;
- 10 X<sub>17</sub>-X<sub>18</sub> is either KF or ST alterations;  
X<sub>19</sub> is either R or a K alteration;  
X<sub>20</sub> is either I or a V alteration;  
X<sub>21</sub> is either T or an S alteration;  
X<sub>22</sub> is either V or a D alteration;
- 15 X<sub>23</sub> is either K or an R alteration;  
X<sub>24</sub> is either A or an E alteration;  
X<sub>25</sub> is either F or a Y alteration;  
X<sub>26</sub>-X<sub>27</sub> is either N or GE alterations;  
X<sub>28</sub>-X<sub>29</sub> is either KE or IH alterations;
- 20 X<sub>30</sub> is either E or a V alteration;  
X<sub>31</sub>-X<sub>32</sub> is either SA or NP alterations;  
X<sub>33</sub> is either F or an Y alteration;  
X<sub>34</sub>-X<sub>35</sub> is either KT or VD alterations;  
X<sub>36</sub>-X<sub>37</sub>-X<sub>38</sub> is either KAE or NLQ alterations;
- 25 X<sub>39</sub> is either N or an E alteration;  
X<sub>40</sub> is either I or a L alteration;  
X<sub>41</sub> is either D or an E alteration;  
X<sub>42</sub> is either E or a D alteration;  
X<sub>43</sub> is either D or a Q alteration;
- 30 X<sub>44</sub> is either K or an R alteration;  
X<sub>45</sub> is either D or an A alteration;  
X<sub>46</sub> is either E or a D alteration;  
X<sub>47</sub> is either I or a V alteration;  
X<sub>48</sub> is either Q or a T alteration;
- 35 X<sub>49</sub> is either E or a D alteration;

- X<sub>50</sub> is either M or an L alteration;  
X<sub>51</sub> is either D or an E alteration;  
X<sub>52</sub>-X<sub>53</sub> is either TK or AH alterations;  
X<sub>54</sub> is either Y or an F alteration;
- 5 X<sub>55</sub> is either Y or an F alteration;  
X<sub>56</sub> is either N or a S alteration;  
X<sub>57</sub> is either M or a V alteration;  
X<sub>58</sub> is either K or an E alteration;  
X<sub>59</sub> is either G or an A alteration;
- 10 X<sub>60</sub> is either M or a T alteration;  
X<sub>61</sub> is either M or a V alteration;  
X<sub>62</sub> is either E or a K alteration;  
X<sub>63</sub> is either D or a S alteration;  
X<sub>64</sub> is either M or an I alteration;
- 15 X<sub>65</sub> is either Q or a K alteration;  
X<sub>66</sub> is either I or a V alteration;  
X<sub>67</sub> is either A or a P alteration;  
X<sub>68</sub> is either T or an S alteration;  
X<sub>69</sub> is either I or a L alteration;
- 20 X<sub>70</sub> is either V or an I alteration;  
X<sub>71</sub> is either T or an A alteration;  
X<sub>72</sub> is either L or a V alteration;  
X<sub>73</sub> is either H or a V alteration;  
X<sub>74</sub> is either D or a G alteration;
- 25 X<sub>75</sub> is either D or an E alteration;  
X<sub>76</sub> is either V or an I alteration;  
X<sub>77</sub> is either E or a D alteration;  
X<sub>78</sub> is either A or an I alteration;  
X<sub>79</sub> is either F or a N alteration;
- 30 provided that at least 20 of said alterations are present.

5. The hybrid polypeptide of claim 4, wherein said modified sequence segment comprises at least 200 amino acids of said modified amino acid sequence.

6. The hybrid polypeptide of claim 5, wherein said modified sequence segment comprises said modified amino acid sequence and at least 55 of said alterations are present.

5 7. The hybrid polypeptide of claim 1, wherein said hybrid polypeptide consists of a sequence selected from the group consisting of SEQ ID NOs: 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, and 43.

10 8. A method of making a hybrid polypeptide comprising the step of introducing one or more alterations into a ORF0657n sequence segment at least about 100 amino acids in length, wherein at least one of said alterations increases sequence similarity to SEQ ID NO: 1.

15 9. An immunogen comprising the modified ORF0657n sequence of claim 1 and one or more additional regions or moieties covalently joined to said sequence at the carboxyl terminus or amino terminus, wherein each region or moiety is independently selected from a region or moiety having at least one of the following properties: enhances the immune response, facilitates purification, or facilitates polypeptide stability.

20 10. A composition able to induce a protective immune response in a patient comprising an immunologically effective amount of the immunogen of any one of claims 1-7 or 9 and a pharmaceutically acceptable carrier.

25 11. The composition of claim 10, wherein said composition further comprises an adjuvant.

30 12. A method of inducing a protective immune response in a patient comprising the step of administering to said patient an immunologically effective amount of the immunogen of any one of claims 1-7 or 9.

13. The method of claim 12, wherein said patient is a human.

35 14. The method of claim 13, wherein said patient is being treated prophylactically against *S. aureus* infection.

15. A nucleic acid comprising a nucleotide sequence encoding the polypeptide of any one of claims 1-7.

16. The nucleic acid of claim 15, wherein said nucleic acid is an expression vector and said nucleotide sequence is part of a recombinant gene.

17. A cell comprising the recombinant gene of claim 16, wherein said recombinant gene expresses said nucleic acid sequence in said cell to produce said polypeptide.

10 18. A method for evaluating the efficacy of an immunogen to produce a protective immune response against *Staphylococcus* comprising the steps of:

(a) inoculating an animal model with said immunogen to produce an immunized animal model;

15 (b) challenging said immunized animal model with a *Staphylococcus* challenge at a potency that provides about 80 to 90% death in said animal model over a period of about 7 to 10 days starting on the first or second day, wherein said *Staphylococcus* challenge is produced from *Staphylococcus* grown to stationary phase, and said *Staphylococcus* challenge is intravenously introduced into said immunized animal model; and

(c) measuring the ability of said immunogen to provide protective immunity.

20 19. The method of claim 18, wherein said *Staphylococcus* is *Staphylococcus aureus*.

25 20. The method of claim 19, wherein said animal model is a rat or mouse.

21. The method of claim 20, wherein said *Staphylococcus* grown to stationary phase is produced on solid media.

22. The method of claim 21, wherein said *Staphylococcus* is grown about 18 30 to 24 hours with a doubling about 20-30 minutes.

23. The method of claim 19, wherein said immunogen is the immunogen of claim 1.